Attorney Docket No.:
TLHR-0005 (124187.00009.US2)

AMENDMENT TO THE CLAIMS

What is Claimed is:

1. (Currently Amended) A method of diagnosing or monitoring a lysosomal storage disorder in a patient, comprising:

obtaining a first sample from the patient; ~~and~~

measuring a first level of at least a first saposin in the first sample obtained from the patient;

comparing the first level to a baseline level, wherein the baseline level is the level of at least the first saposin as determined in a control population of patients unaffected by the lysosomal storage disorder; and

determining a presence or extent of a lysosomal storage disorder when the first level is similar or different than the 95th percentile of the baseline level of at least the first saposins in the control population;

wherein,

~~(i) the first level is similar or different from the baseline level;~~

(i) the similarity of the first level compared to the baseline level is an indicator of absence of the lysosomal storage disorder in the patient;

(ii) the difference of the first level compared to the baseline level is an indicator of presence or extent of the lysosomal storage disorder in the patient;

(iii) the first saposins comprises saposin A, saposin B, saposin C, saposin D, ~~prosaposin, mRNA encoding prosaposin,~~ or a combination thereof; and

(iv) the first sample is a plasma, serum, whole blood, urine, or amniotic fluid sample.

2. (Canceled) ~~The method of claim 1, wherein the first sample is a plasma sample.~~

3. (Canceled) ~~The method of claim 1, wherein the first sample is a whole blood sample.~~

4. (Currently Amended) The method of claim 1, further comprising indicating a presence of the lysosomal disorder in the patient when the first level exceeds the baseline level. ~~wherein a presence of the lysosomal disorder in the patient, is indicated by the first level exceeding the baseline level.~~

5. (Currently Amended) The method of claim 1, further comprising:

measuring a second level of ~~the~~ a second saposin in a second sample from the patient, wherein the first saposin and second saposin are the same, and the first and second samples ~~being~~ are obtained at different times; and

comparing the first level and the second level in the samples to monitor progression of the disease,

determining a presence or extent of a lysosomal storage disorder when the second level is similar or different than the 95th percentile of the baseline level of at least the two saposins in the control population;

wherein,

(i) the second saposin comprises saposin A, saposin B, saposin C, saposin D ~~prosaposin, mRNA encoding prosaposin,~~ or a combination thereof;

(ii) the comparison of the first level and the second level is an indicator of the progression of the disease in the patient; and

(iii) the second sample is a plasma, serum, whole blood, urine, or amniotic fluid sample.

6. (Currently Amended) The method of claim 1, ~~wherein the patient~~ further comprising selecting the patient that is undergoing treatment for the lysosomal storage disorder.

7. (Canceled) ~~The method of claim 4, wherein the first level is greater than the 95th percentile of the baseline level in the control population.~~

8. (Currently Amended) The method of claim 1, ~~wherein the patient~~ further comprising selecting the patient that is not known to have a lysosomal storage disorder before the measuring step.

9. (Currently Amended) The method of claim 1, ~~wherein the patient~~ further comprising selecting the patient that is an infant less than one year old.

10. (Currently Amended) The method of claim 1, further comprising selecting the patient that ~~wherein the patient~~ is a fetus and the sample is a fetal blood sample.

11. (Previously Presented) The method of claim 5, wherein a change in the first level of the saposin indicates progression or regression of the disorder in the patient that is known to have a lysosomal storage disorder.

12. (Previously Presented) The method of claim 5, wherein a change in the first level of the saposin indicates a response to treatment of the lysosomal storage disorder in the patient that being treated for the lysosomal storage disorder.

13. (Canceled) ~~The method of claim 5, wherein the first saposin or second saposin is selected from the group consisting of saposin A, saposin B, saposin C, and saposin D.~~

14. (Canceled) ~~The method of claim 1, wherein the saposin is selected from the group consisting of saposin A, saposin C, or saposin D.~~

15. (Previously Presented) The method of claim 1, wherein the measuring step comprises detecting binding between a saposin polypeptide and an antibody.

16. (Original) The method of claim 15, wherein the antibody is a monoclonal antibody.

17. (Original) The method of claim 15, wherein the antibody is immobilized to a solid phase.

18. (Currently Amended) The method of claim 1, wherein the lysosomal storage disorder is selected from the group consisting of cystinosis, Fabry's disease, Niemann-Pick disease, Pompe's disease, Wolman disease~~, and subset thereof~~.

19. (Original) The method of claim 1, further comprising informing the patient or a parent or guardian thereof of the presence of the lysosomal storage disorder.

20. (Previously Presented) The method of claim 1, further comprising determining a treatment program based on the measurement of the first level of the first saposin.

21. (Withdrawn) A method of diagnosing or monitoring a lysosomal storage disorder in a patient, comprising: measuring the level of a-glucosidase in a tissue sample from a patient, wherein the level is an indicator of the presence or extent of the disorder in the patient.

22. (Withdrawn) The method of claim 21, wherein the sample is a plasma sample.

23. (Withdrawn) The method of claim 21, wherein the sample is a blood sample.

24. (Withdrawn) The method of claim 21, further comprising diagnosing the presence of a disorder selected from the group consisting of acid lipase disease, mannosidosis, MPSII, MPS IIIA, MSD, mucolipidosis, N-P (A/B), N-P (C), Sandhoff, SAS or TSD B1, if the measured level of a-glucosidase exceeds the mean level in a control population of individuals not having a lysosomal storage disease.

25. (Withdrawn) The method of claim 21, further comprising diagnosing the presence of disorder selected from the group consisting of galactosialidosis, MPS IVA and Pompe's disease if the measured level of a-glucosidase is below the mean level in a control population of individuals not having lysosomal storage disease.

26. (Withdrawn) A method of diagnosing a lysosomal storage disorder comprising measuring a level of a saposin in a tissue sample from the patient; measuring a level of LAMP-1 or LAMP-2 in a second tissue sample from the patient; measuring a level of a glucosidase in a third tissue sample from the patient; wherein an increased level of saposin and/or LAMP-1 or LAMP-2, and/or an increased or decreased level of a-glucosidase in the sample relative to respective mean levels in a control population is an indicator of presence or extent of the disorder in the patient.

27. (Withdrawn) A method of diagnosing Pompe's disease in a patient, comprising measuring a level of a saposin in a tissue sample from the patient: measuring the level of a-glucosidase in a second tissue sample from the patient; wherein the presence of an increased level of the saposin and a decreased level of the a-glucosidase relative to mean levels of the saposin and a-glucosidase in a control population of individuals not having a lysosomal storage disorder indicates Pompe's disease or susceptibility thereto.

28. (Withdrawn) A method of screening patients for presence of lysosomal storage disorder, comprising: measuring the level of a LAMP-1 polypeptide in a sample from the patient: measuring the level of a saposin peptide in the sample, the presence of an increased level of LAMP-1 or saposin or both relative to mean levels in a control population, indicating susceptibility to a lysosomal disorder.

29. (Withdrawn) A diagnostic kit comprising: a first reagent that binds to a LAMP; a second reagent that binds to a saposin.

30. (Withdrawn) The diagnostic kit of claim 29, further comprising a third reagent that binds to a glucosidase.

31. (Withdrawn) The diagnostic kit of claim 30, wherein the first, second and third reagents are antibodies.

32. (Withdrawn) In a method of screening a patient for presence or susceptibility to disease, comprising performing a plurality of diagnostic tests on a tissue sample from the patient for a plurality of diseases, the improvement wherein one of the diagnostic tests comprises measuring the level of a saposin.

33. (Withdrawn) In the method of claim 32, the further improvement wherein a second of the diagnostic tests comprising measuring the level of LAMP-1 in the tissue sample from the patient.

34. (Withdrawn) In the method of claim 33, the further improvement wherein a third of the diagnostic tests comprises measuring the level of a-glucosidase in the tissue sample from the patient.

35. (Withdrawn) In the method of claim 32, the further improvement wherein a fourth of the diagnostic test comprises analysing a nucleic acid encoding an enzyme associated with a lysosomal storage disorder for a polymorphic form correlated with the disorder.

36. (Previously Presented) A method of monitoring treatment of a lysosomal storage disease in a patient, comprising:

determining a pre-treatment baseline level of a saposin in a sample from the patient with a lysosomal storage disorder before treatment with an agent;

determining a post-treatment baseline level of the saposin in a sample from the patient with the lysosomal storage disorder after treatment with the agent; and

comparing the pre-treatment baseline level of the with the post-treatment baseline level of the saposin, wherein

(i) the sample is a plasma, serum, whole blood, urine, amniotic fluid sample, or a mixture of;

(ii) saposin is selected from the group consisting of saposin A, saposin B, saposin C, saposin D, ~~prosaposin, mRNA encoding prosaposin, and a combination thereof~~; and

(iii) a reduction in the post-treatment baseline level relative to the pre-treatment baseline level indicates a positive treatment outcome.

37. (Withdrawn) A method of monitoring treatment of acid lipase disease, mannosidosis, MPSII, MPS IIIA, MSD, mucolipidosis, N-P (A/B), N-P (C), Sandhoff, SAS or TSD B1, comprising: determining a baseline level of a glucosidase in a tissue sample from the patient with the disorder before treatment with an agent; comparing a level of the a glucosidase in a tissue sample from the patient with the disorder after treatment with the agent with the baseline level; wherein a decrease relative to the baseline indicates a positive treatment outcome.

38. (Withdrawn) A method of monitoring a patient with Pompe's disease, comprising: determining a baseline level of a glucosidase in a tissue sample from the patient with the disorder before treatment with the agent; comparing a level of the a-glucosidase in a tissue sample from the patient after treatment with the agent with the baseline level; wherein an increase relative to the baseline indicates a positive treatment outcome.

39. (New) A method of diagnosing or monitoring a lysosomal storage disorder in a patient, comprising:

obtaining a first sample from the patient;

measuring a first level of a saposin in the first sample obtained from the patient;

comparing the first level to a baseline level, wherein the baseline level is the level of the saposin as determined in a control population of patients unaffected by the lysosomal storage disorder;

determining a presence or extent of a lysosomal storage disorder when the first level is similar or different than the 95th percentile of the baseline level of at least the two saposins in the control population;

wherein,

(i) the similarity of the first level compared to the baseline level is an indicator of absence of the lysosomal storage disorder in the patient;

(ii) the difference of the first level compared to the baseline level is an indicator of presence or extent of the lysosomal storage disorder in the patient;

(iii) the saposin comprises saposin A, saposin B, saposin C, saposin D;

(iv) the first sample is plasma; and

(v) the baseline level and the first level are about equal to a percent elevation level for the lysosomal storage disorder listed in Table 2.